



Selección de Resúmenes de Menopausia

Semana del 13 al 19 de Junio de 2018

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Bone. 2018 Jun 13. pii: S8756-3282(18)30239-4. doi: 10.1016/j.bone.2018.06.007. [Epub ahead of print]

Prevention of breast cancer treatment-induced bone loss in premenopausal women treated with zoledronic acid: Final 5-year results from the randomized, double-blind, placebo-controlled ProBONE II trial.

Kyvernitakis I, Kann PH, Thomasius F, Hars O, Hadji P.

PURPOSE: Premenopausal women receiving chemotherapy or endocrine treatment for early breast cancer are at increased risk for cancer treatment induced bone loss (CTIBL). The aim of the randomized, double-blind ProBONE II trial was to investigate whether a 2-year adjuvant treatment with 4 mg intravenous zoledronic acid (ZOL) every 3 months versus placebo would prevent CTIBL after a five-year period. **METHODS:** Thirty-one of the 34 participants in the ZOL arm and thirty-four of the 36 participants in the placebo arm were followed-up to the 5-year visit and completed the study as planned. The changes in Bone Mass Density (BMD) were assessed at baseline and each visit after treatment initiation. **RESULTS:** After 24 months, BMD at the lumbar spine showed a 2.9% increase in patients treated with ZOL vs. a 7.1% decrease in placebo-treated participants compared to baseline ($p < 0.001$). Over the 60-month study period, we found a decrease of 2.2% vs. 7.3% in the BMD at the lumbar spine in patients receiving ZOL and placebo respectively ($p < 0.001$). Over the 60-month study period, BMD in the placebo arm showed a continuous decrease at all sites ($p < 0001$), whereas patients treated with ZOL reached baseline BMD-values at the femoral neck and total hip. **CONCLUSIONS:** In ProBone II, a 2-year treatment with ZOL 4 mg intravenous every 3 months prevented cancer treatment induced bone loss in premenopausal women with breast cancer and maintained the BMD up to 3 years post-treatment.

Maturitas. 2018 Aug;114:60-66. doi: 10.1016/j.maturitas.2018.06.004. Epub 2018 Jun 5.

Micro-RNA-181a suppresses progestin-promoted breast cancer cell growth.

Gu M, Wang L, Yang C, Li X, Jia C, Croteau S, Ruan X, Hardy P.

BACKGROUND: Recent investigations have indicated that hormone therapy may increase the risk of breast cancer (BC), and the addition of synthetic progestins may play a critical role in this. Several studies have pointed out the important role of progesterone receptor membrane component 1 (PGRMC1) in the development of BC, especially with hormone therapy using progestins. Although the deregulation of microRNA-181a (miR-181a) is often associated with human BC, the effect of miR-181a on PGRMC1 expression during hormone therapy has not been investigated. **METHODS:** Cell viability assay and apoptosis assay were performed to investigate the pro-BC effect of progestin (norethisterone, NET) and anti-BC effect of miR-181a on MCF-7 cells. Quantitative RT-PCR and Western blot analysis were used to evaluate gene expressions in the NET-treated MCF-7 cells. **RESULTS:** NET dose-dependently increased BC cell viability and this effect was accompanied by increased expression of PGRMC1. Overexpression of miR-181a strongly reduced the cell viability of MCF-7 cells, mainly through increased apoptosis, which was evidenced by substantially increased gene expression of pro-apoptosis factors such as BAX and CASPASE 9 in miR-181a overexpressed cells. Importantly, miR-181a abrogated NET-stimulated cell viability and PGRMC1 expression. **CONCLUSIONS:** We provide evidence that miR-181a promotes MCF-7 cell apoptosis. Moreover, miR-181a suppressed NET-provoked cell viability and PGRMC1 expression in MCF-7 cells. These data may suggest a therapeutic strategy of using miR-181a to reduce BC risk in progestin hormone replacement therapy.

Int J Gynaecol Obstet. 2018 Jun 15. doi: 10.1002/ijgo.12567. [Epub ahead of print]

Comparison of endometrial assessment by transvaginal ultrasonography and hysteroscopy.

Yela DA, Pini PH, Benetti-Pinto CL.

OBJECTIVE: To compare transvaginal ultrasonography and hysteroscopy for the diagnosis of endometrial pathologies. **METHODS:** In the present retrospective cohort study, data were reviewed from women with ultrasonography findings suggestive of endometrial lesions and/or abnormal uterine bleeding who underwent

hysteroscopy at a single center in Campinas, Brazil, between January 2011 and December 2013; data were stratified based on reproductive-aged and postmenopausal groups. The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ultrasonography and hysteroscopy for the diagnosis of endometrial lesions were determined. Histopathology was used as the gold standard. RESULTS: There were 754 patients included (256 reproductive age, 498 postmenopausal). In the reproductive-age group, ultrasonography had a sensitivity of 96.0%, specificity of 58.0%, PPV of 94.4%, NPV of 66.6%, and accuracy of 91.5%, whereas hysteroscopy had a sensitivity of 91.8%, specificity of 76.6%, PPV of 96.0%, NPV of 60.5%, and accuracy of 89.7% for the diagnosis of endometrial disease. In the postmenopausal group, ultrasonography had a sensitivity of 99.0%, specificity of 19.0%, PPV of 96.1%, NPV of 50.0%, and accuracy of 95.3%, whereas hysteroscopy had a sensitivity of 96.7%, specificity of 86.9%, PPV of 99.2%, NPV of 58.8%, and accuracy of 96.2%. CONCLUSION: Ultrasonography was found to be an effective method for the diagnosis of endometrial disease, especially among postmenopausal women.

Eur J Phys Rehabil Med. 2018 Jun 14. doi: 10.23736/S1973-9087.18.05191-2. [Epub ahead of print]

Classes of vitamin D status and functional outcome after hip fracture: a prospective, short-term study of 1350 inpatients.

Di Monaco M, Castiglioni C, Di Carlo S, La Marmora E, Filipovic I, Milano E, Minetto MA, Massazza G.

BACKGROUND: Vitamin D depletion is associated with unfavourable outcomes after hip fracture. However, the classes of vitamin D status currently in use, which are defined according to serum calcifediol levels, have not been validated for their predictive capability of the functional recovery. AIM: To investigate the association between serum calcifediol categorized into 4 classes and the functional recovery after hip fracture. DESIGN: Prospective, short-term observational study. SETTING: Rehabilitation hospital in Italy. POPULATION: We evaluated 1350 of 1412 inpatients with hip fracture. METHODS: Serum calcifediol was measured by an immunoenzymatic assay 14.7 ± 4.4 (mean \pm SD) days after surgery and categorized into 4 classes: I class <12 ng/ml; II class 12-20ng/ml; III class 21-29ng/ml; IV class ≥ 30 ng/ml. The functional outcome was assessed by using the Barthel index. RESULTS: We found a significant difference in Barthel index scores at the end of inpatient rehabilitation across the 4 classes of vitamin D status: $\square 2$ (3, n=1350) 27.2; $p < 0.001$. The difference persisted after adjustment for 8 covariates ($p = 0.004$). By comparing pairs of classes, we found that Barthel index scores were lower in the 829 patients of the I class than in the 275 of the II ($p = 0.005$) who had in turn Barthel index scores lower than the 132 patients of the III class ($p = 0.038$). Conversely, no significant differences emerged between the patients of the III class and the 114 patients of the IV class ($p = 0.421$). The results did not materially change when Barthel Index effectiveness was substituted for Barthel Index scores as the outcome measure. CONCLUSIONS: Calcifediol levels below 12ng/ml were associated with a worse recovery than those between 12 and 20ng/ml that were in turn associated with a worse recovery than those between 21 and 29ng/ml. Conversely, no significant differences were found between the patients with calcifediol between 21 and 29ng/ml and those with calcifediol ≥ 30 ng/ml. CLINICAL REHABILITATION IMPACT: Despite caution due to the observational design, our study suggests that vitamin D depletion should be treated after hip fracture to optimize the functional outcome, with a target level for serum calcifediol of 21-29ng/ml and no further advantages associated with calcifediol levels of 30ng/ml or higher.

Maturitas. 2018 Jul;113:21-25. doi: 10.1016/j.maturitas.2018.04.006. Epub 2018 Apr 18.

High parathyroid hormone levels are associated with osteosarcopenia in older individuals with a history of falling.

Suriyaarachchi P, Gomez F, Curcio CL, Boersma D, Murthy L, Grill V, Duque G.

OBJECTIVES: The combination of osteopenia/osteoporosis and sarcopenia (osteosarcopenia) defines a diagnostic subset of individuals at higher risk of falls, fractures and institutionalization. In this study we aimed to assess the potential role of high serum levels of parathyroid hormone (PTH) in osteosarcopenia. We hypothesized that a high PTH level is one of the major determinants of this syndrome. STUDY DESIGN: Cross-sectional study in 400 subjects (mean age = 79, 65% women) assessed between 2009 and 2014 at the Falls and Fractures Clinic, Nepean Hospital (Penrith, Australia). MAIN OUTCOME MEASURES: Medical history, physical examination, bone densitometry, body composition, posturography, grip strength, gait parameters, and blood tests for nutrition and secondary causes of sarcopenia and osteoporosis. Patients were assigned to one of four groups: 1) osteopenic/osteoporotic; 2) sarcopenic; 3) osteosarcopenic; or 4) non-sarcopenic/non-osteopenic. Patients with

abnormal corrected calcium levels were excluded from analysis. Between-group differences were assessed using one-way analysis of variance and chi-squared tests. Multivariable linear regression was used to evaluate the association between the groups and PTH levels adjusted for age, vitamin D, renal function and albumin. **RESULTS:** 24% of the subjects had a high serum PTH level with normal corrected calcium level. These subjects were older, reported more falls per year, and had lower grip strength, limits of stability, BMD, and gait velocity. Subjects with high PTH levels were more likely to be in the osteosarcopenia group than in the non-sarcopenic/non-osteopenic group (OR 6.88; CI: 1.9-9.2). **CONCLUSIONS:** We reported an independent association between high PTH levels and osteosarcopenia. Our results suggest an important role of PTH in osteosarcopenia that deserves further exploration.

J Med Assoc Thai. 2016 Oct;99 Suppl 7:S93-8.

Atherosclerotic Index and Traditional Anthropometry for Predicting Carotid Intima Media Thickness in Perimenopausal/Menopausal Women.

Nimkuntod P, Tongdee P.

Background: Atherosclerosis is an important pathologic cause of cardiovascular disease (CVD) and a leading cause of morbidity and mortality worldwide. Menopause involves changes in hormonal status that are associated with an increased risk of developing CVD. The atherogenic index of plasma (AIP) has been used as a predictor of atherosclerosis. Atherosclerosis might also be assessed using a surrogate marker, the carotid artery wall intima media thickness (CIMT). **Objective:** To assess the usefulness of AIP compared with traditional anthropometrics for predicting CIMT in perimenopausal and menopausal women. **Material and Method:** This is a cross-sectional study involving perimenopausal and menopausal women voluntarily recruited. Lipid profiles, including total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were assessed and AIP was calculated [$\log(TG/HDL-C)$]. The anthropometric parameters of body mass index (BMI), waist circumference (WC), hip circumference (HC), and waist-hip ratio (WHR) were assessed. Pearson Chi-square for AIP and anthropometric parameters relationship to CIMT in perimenopausal and menopausal women. **Results:** One hundred fourteen perimenopausal and menopausal women were included in this study. The novel atherosclerotic index of AIP and the anthropometric parameter of BMI were correlated with CIMT in both groups ($p < 0.01$). There was no difference in AIP between perimenopausal and menopausal women. Neither WC nor WHR were different between the two groups. CIMT was significantly thicker in the menopausal compared with the perimenopausal group [0.78 ± 0.16 vs. 0.64 ± 0.09 , respectively ($p < 0.01$)]. **Conclusion:** AIP can add significant value when assessing the risk of developing the atherosclerosis marker of thickened CIMT in perimenopausal and menopausal women. A high AIP in menopause may indicate a higher risk of cardiovascular events in spite of no difference in common CVD risk factors such as lipid profile parameters.

Can Fam Physician. 2018 Jun;64(6):433-438.

Management of bone health in patients with celiac disease: Practical guide for clinicians.

Duerksen D, Pinto-Sanchez MI, Anca A, Schnetzler J, Case S, Zelin J, Smallwood A, Turner J, Verdú E, et al.

OBJECTIVE: To describe clinical issues related to bone health in patients with celiac disease (CD) and to provide guidance on monitoring bone health in these patients. **SOURCES OF INFORMATION:** A PubMed search was conducted to review literature relevant to CD and bone health, including guidelines published by professional gastroenterological organizations. **MAIN MESSAGE:** Bone health can be negatively affected in both adults and children with CD owing to the inflammatory process and malabsorption of calcium and vitamin D. Most adults with symptomatic CD at diagnosis have low bone mass. Bone mineral density should be tested at diagnosis and at follow-up, especially in adult patients. Vitamin D levels should be measured at diagnosis and annually until they are normal. In addition to a strict gluten-free diet, supplementation with calcium and vitamin D should be provided and weight-bearing exercises encouraged. **CONCLUSION:** Bone health can be adversely affected in patients with CD. These patients require adequate calcium and vitamin D supplementation, as well as monitoring of vitamin D levels and bone mineral density with regular follow-up to help prevent osteoporosis and fractures.